

Composition Exhibiting a von Willebrand Factor (vWF) Protease Activity Comprising a Polypeptide Chain with the Amino Acid Sequence AAGGILHLELLV

*10001] This application is a continuation-in-part of US application number 09/721,254*

*03/31/00 filed on November 22, 2000, now abandoned.*

*Ind* **FIELD OF THE INVENTION**

*10002] The invention relates to a vWF protease-containing composition which includes a polypeptide comprising the amino acid sequence AAGGILHLELLV, as well as to nucleotide sequences coding for such a polypeptide. It further relates to methods for increasing the stability of the vWF protease.*

**BACKGROUND OF THE INVENTION**

**10003]** vWF is a glycoprotein circulating in plasma as a series of multimers ranging in size from about 500 to 20,000 kD. Multimeric forms of vWF are composed of 250 kD polypeptide subunits linked together by disulfide bonds. vWF mediates the initial platelet adhesion to the subendothelium of a damaged vessel wall, though only the largest multimers appear to exhibit haemostatic activity. Such vWF multimers having large molecular masses are stored in the Weibel Palade bodies of endothelial cells, and it is believed that endothelial cells secrete these large polymeric forms of vWF. Those forms of vWF which have a low molecular weight (low molecular weight or LMW vWF) are believed to arise from proteolytic cleavage of the larger multimers.

**10004]** A small portion of the vWF present in normal plasma circulates as 189, 176 and 140 kD fragments resulting from proteolytic degradation of vWF *in vivo*, the 140 kD fragment being derived from the N-terminal region, and the 176 kD fragment from the C-terminal region of the subunit. When LMW forms of vWF are isolated from normal human plasma and subjected to SDS-PAGE (polyacrylamide gel electrophoreses) after disulfide reduction, an unusually high portion of vWF fragments are found. This finding is